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EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/604,022	COLLINS ET AL.	
	Examiner	Art Unit	
	Marcela M. Cordero Garcia	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1.2 and 4-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/07 and 02/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the reply received on February 15, 2007.

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Claims 1-2 and 4-12 are pending in the application.

Any rejection from the previous office action, which is not restated here, is withdrawn.

Applicant has now amended the base claim to recite synthesis in a single *microwave transparent* vessel. Claims 1-2 and 4-12 are presented for examination on the merits.

New Grounds for rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 4-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The MPEP states that the purpose of the

written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by

structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

In the instant case, the claims are drawn to a process for the solid phase synthesis of peptides which comprises:

(a) deprotecting a first amino acid linked to a solid phase resin by removing protective chemical groups from said first acid;

(b) activating chemical groups on a second amino acid to prepare the second amino acid for coupling with the first amino acid;

(c) coupling the activated second amino acid to the deprotected first amino acid to form a peptide from the first and second amino acids;

(d) accelerating at least the deprotecting and coupling steps by applying microwave energy during the deprotecting, and coupling steps; and

(e) successively deprotecting, activating and coupling a plurality of amino acids into a peptide in a single microwave transparent vessel without removing the peptide from the single vessel between cycles.

With regards to the "microwave transparent" term, this is a very broad generic statement, which is not well defined beyond some examples in the specification (e.g., glass, polyethylene, Teflon, PTFE variations). The specification does not disclose if, e.g., the transparency needs to be over the whole microwave electromagnetic region or within a particular region of the microwave spectrum (such as in cooking microwave ovens) or if it is sufficient to minimally absorb at some region but transmit in another

within the microwave range of electromagnetic radiation, and it encompasses many other compounds which are not susceptors or which contain both transparent and susceptor areas are not adequately described and/or represented in the examples. By the same token, the term "vessel", which is also not defined, is extremely broad, with many different configurations, shapes and sizes including, tubes, wells, cylinders, plastic bags, semi-flexible containers, surface carriers and so forth, which are encompassed by the term "vessel" and for which no adequate examples are provided. The claims are drawn to a process of the solid phase synthesis of peptides comprising a series of steps in a single microwave transparent vessel without removing the peptide from the single vessel between the cycles, therefore a mere statement that any vessels would be desirable for such reactive synthesis does not sufficiently provide ample written description pages describing the full breadth of the single microwave transparent vessels with the capability claimed. The specification does provide examples of what qualify as embodiments of the claimed invention (see, e.g, disclosure, [0040]-[0043] and Figures 3-4), however, these are limited to a single type of microwave transparent vessel of specific shape and constructed in PTFE, PTFE variations or polypropylene. Please note that there is not limiting definition for vessel, and that vessel is not exemplified beyond the examples in Figures 3-4 which describe a single shape of vessel. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic with respect all possible microwave transparent reaction vessels encompassed by the claims. The possible structural variations are virtually limitless to any class of microwave transparent reaction vessel suitable for microwave solid peptide synthesis within the instantly claimed process. Here, though the claims may recite some functional characteristics, the claims lack

written description because there is no disclosure of a correlation between function and structure of the claimed vessels beyond the vessel disclosed in the Figures in the specification for the claimed synthetic method. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of other microwave transparent vessels such as vials, wells, cylinders, glasses, containers of any shape, mixed material containers (e.g., partly transparent and partly susceptor) and so forth. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

New rejection under 102(a) and (e)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1 and 4 are rejected under 35 U.S.C. 102(a) or under 102(e) as being anticipated by Martin et al. (US 2003/0082633) as evidenced by Hilpert et al. (Protein Engineering, 2001).

Martin et al. teach a process for the solid phase synthesis of peptides (EQKLISEEDL and EQKHISEEDL) in a single vessel (e.g., Example 12-13) and shortening reaction times by a factor of 2-20 fold by the use of the microwave energy during the reactions (e.g., Example 12, [0294]-[0300]). Hilpert et al. teach that the peptides of Martin et al. were synthesized via a cellulose-bound C-terminus with two β-alanine as a spacer (e.g., column 2, lines 16-18) and following a protection/deprotection scheme (e.g., column 2, lines 12-17) and therefore would inherently encompass the instantly claimed standard solid phase peptide synthetic steps. Please note that the

limitation "in a single vessel without removing the peptide from the single vessel between cycles" is met by the fact that the peptides are chemically bound to the cellulose during synthesis (e.g., Martin et al. Example 12, [00295], lines 1-8), which is glued on top of a sandwich comprising two standard glass microscope slides (a microwave transparent material) and the edges are sealed to enclose barium titanate (a microwave susceptor). The vessel therefore reads upon a microwave transparent vessel and upon a microwave susceptor vessel. Therefore, the reference is deemed to anticipate the instant claims above.

Applicant argues that the reference does not enable the subject matter for which it is being asserted because the disclosure in the anticipating reference incorporates the Hilpert reference (which incorporates Kramer and Kramer-Schneider (see PTO 892) and the Sigma-Genosys technical notes, and since there is a large number of permutations that arise from Martin '633 with the references incorporated by reference Hilpert, Sigma-Genosys and subsequently Kramer and Kramer-Schneider and therefore the Martin '633 publication cannot enable the claimed invention and thus must fail as prior art for such purpose. Applicant also argues that the claim 1 has been amended to recite that the single vessel is "microwave transparent" distinguishing from Martin's microwave-absorbing susceptor and thus claim 1 is not disclosed within its four corners.

Applicant's arguments have been considered and have not been deemed persuasive because of the reasons cited above and because one of ordinary skill in the art would understand how to use the claimed invention based on the skill in the art

regarding solid phase synthesis and upon the disclosure of Martin and the guidance provided, including citations therein. In addition, a definition of "microwave transparent vessel" is not provided by the specification, therefore the term "vessel" reads upon any container (see http://answers.com/vessel, accessed online 3/13/07, see, e.g., Word Tutor section and WordNet Meaning #3). Merabet (US 6,486455) teaches that glass is microwave transparent (e.g., column 6, lines 40-45). Therefore the "sandwich dielectric chip" made of two glass slides and titanate reads upon a microwave transparent vessel upon (since it contains a microwave transparent material, i.e., glass) upon which the solid phase (the cellulose membrane) with the peptide is contained. Please also note that the cellulose (a microwave transparent material as taught by Merabet, column 6, lines 40-45) is a constituent of the solid phase peptide synthesis as taught by Martin (e.g. Example 12, [00295], lines 1-8),

Rejections maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004) in view of Williams (US 6,858,434) and in view of Martin et al. (US 2003/0082633).

Yu et al. teach a process for the solid phase synthesis of peptides, which comprises:

(a) deprotecting a first amino acid linked to a solid phase resin by removing protective first chemical groups;

(b) activating chemical groups on a second amino acid to prepare the second amino acid for coupling with the first amino acid;

c) coupling the activated second amino acid to the deprotected first amino acid to form a peptide from the first and second amino acids; and

(d) accelerating at least the coupling step by applying microwave energy during the coupling step. (see, e.g., page 4782-4784, Figures 1-2 and Scheme 1).

Yu et al. do not teach accelerating the deprotecting step by applying microwave energy during the deprotecting step or carrying out the reaction in a single vessel without removing the peptide from the single vessel between cycles.

Williams teaches deprotecting n-Boc protected amino acids by applying microwave energy during the deprotecting step (e.g., Example 5).

Martin et al. is relied upon as above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the solid phase microwave method of Yu et al. by carrying out the reaction on a cellulosic membrane to which the peptide to be

synthesized is attached, as taught by Martin et al. (See, e.g., [294]-[301]) and accelerating the synthesis steps including deprotecting steps (as taught by Williams) with microwaves (See, e.g., Martin et al., column 23, [294]-[301]). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods-- substantially accelerate reactions and save time as taught by Yu et al. (page 4781, column 1, lines 13-15) and by Williams (Example 5). There would have been a reasonable expectation of success, given the successful synthesis in a single microwave transparent vessel of the peptides: EQKLISEEDL and EQKHISEEDL as taught by Martin et al. (e.g., Examples 12-13). Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 2, 5, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004) (Tetrahedron Letters, 2001) in view of Stadler et al. (Eur J Org Chem, 2001) in view of Santagada et al. (Tetrahedron Letters, 2001, citation 4 in the IDS of November 8, 2004) and in view of Martin et al. (US 2003/0082633).

Yu et al., Williams and Martin et al. are relied upon as above.

Yu et al. Williams and Martin et al. do not expressly teach accelerating the deprotecting step by applying microwave energy during the deprotecting step, maintaining the peptide in a single vessel during the process proactively cooling the vessel and its contents during application of microwave energy, cleaving the peptide

from the resin applying microwave energy, deprotecting side chains of the peptide, spiking the microwave energy, using phosphorium activators, uranium activators, HATU, HBTU, PyBOP, PyAOP or HOBT, monitoring the temperature of the vessel and moderating the applied power accordingly.

Stadler et al. teach cleaving various molecules including carboxylic acids from resins by applying microwave energy, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly (see, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2).

Santagada et al. teach using PyBOP/HOBt and HBTU/HOBt activators in a microwave method for peptide synthesis (see, e.g., pages 5171-5173).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the microwave method of Yu et al. by also accelerating the deprotecting steps in general during peptide synthesis with microwaves based on the teachings of Williams (See, e.g., Examples 5 and 7), by accelerating the cleavage from the solid-support resin as taught by Stadler et al. (See, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2), and by using activators such as PyBOP/HOBt and HBTU/HOBt during microwave activation, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly, as taught by Santagada et al. (See, e.g., pages 5171-5173). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in

comparison to conventional heating methods-- substantially accelerate reactions and save time (e.g., Yu et al. page 4781, column 1, lines 13-15) and provide higher yields (e.g., Santagada et al. abstract). There would have been a reasonable expectation of success, given the successful synthesis in a single microwave transparent vessel of the peptides: EQKLISEEDL and EQKHISEEDL as taught by Martin et al. (e.g., Examples 12-13). The adjustment of particular conventional working conditions (e.g., deprotecting protective groups other than n-Boc in peptides, and alpha-amino groups or side chains of the peptide) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicant argues claim 1 now specifically recites that the single vessel is a microwave transparent vessel and that this is functionally opposite from Martin's susceptor plate which incorporates barium titanate between two standard glass microscope slides in order to absorb rather than transmit microwaves ([0295]). Applicant's arguments have been considered yet not deemed persuasive because the vessel does transmit microwaves (the glass part of the vessel) and there is no definition provided which excludes vessels combining both transparent and susceptor materials such as the glass/barium titanate combination, which at least in part is a transparent vessel.

Applicant also argues that the combination of reference cited collapses because the three techniques (Yu, Williams and Martin) fundamentally differ from one another and cannot be logically combined other than as an attempt to reconstruct claim 1 because Yu uses solid phase HMP resin, Williams uses thin layer TLC coated with silica gel and accordingly there is no suggestion as to why Williams technique ought to be carried out on an HMP resin or why the Williams technique ought to be carried out on an HMP resin or why the Yu technique ought to be modified to incorporate silica gel instead of a solid phase. Applicant's arguments have been considered yet not deemed persuasive because as taught by each of the references, microwave energy accelerates reactions independently of the substrate wherein the synthesis is carried out and because Martin teaches microwave fast total synthetic speeds for peptides, which therefore necessarily reads upon microwave activation of the synthetic steps as claimed.

Applicant argues as well that Martin does not read upon a "single vessel" and that the term "cellulose membrane" does not read upon "solid phase" because it requires Martin's cellulose membrane to serve as both the linked solid phase resin and the microwave transparent single vessel. Applicant's arguments have been considered yet not deemed persuasive because the instant disclosure does not limit the term "solid phase" to a specific type of support (e.g., [0011]-[0012]) and because Martin et al. teach solid phase peptide synthesis, specifically, the cellulose membrane has four acceptor spots for peptide synthesis and the solid phase is used as a scaffold on which molecules are built which reads upon solid phase synthesis (e.g., [0294]-[0295]). In

addition, the term "vessel" reads upon any container (see http://answers.com/vessel, accessed online 3/13/07, see, e.g., Word Tutor section and WordNet Meaning #3). The "sandwich dielectric chip" reads therefore upon a container upon which the solid phase (the cellulose membrane) with the peptide is contained.

New Rejections

Claim Rejections - 35 USC § 103

Claim 1 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004) in view of Williams (US 6,858,434) and in view of Cargill et al. (US 6,171,555).

Yu et al. teach a process for the solid phase synthesis of peptides, which comprises:

(a) deprotecting a first amino acid linked to a solid phase resin by removing protective first chemical groups;

(b) activating chemical groups on a second amino acid to prepare the second amino acid for coupling with the first amino acid;

c) coupling the activated second amino acid to the deprotected first amino acid to form a peptide from the first and second amino acids; and

(d) accelerating at least the coupling step by applying microwave energy during the coupling step. (see, e.g., page 4782-4784, Figures 1-2 and Scheme 1).

Yu et al. do not teach accelerating the deprotecting step by applying microwave energy during the deprotecting step or carrying out the reaction in a single vessel without removing the peptide from the single vessel between cycles.

Williams teaches deprotecting n-Boc protected amino acids by applying microwave energy during the deprotecting step (e.g., Example 5).

Cargill et al. teach a process for the solid phase synthesis of peptides in a single vessel (column 1, lines 38-67; column 2 and column 3, lines 1-30) using microwaves (e.g., column 4, lines 37-39) in a single microwave transparent vessel (e.g., column 4, lines 15-24, Figures 1; column 4, lines 25-39, Figure 2 and column 4, lines 43-67).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the solid phase microwave method of Yu et al. by carrying out the reaction in a single microwave transparent vessel as taught by Cargill et al. (e.g., column 4, lines 15-24, Figures 1; column 4, lines 25-39, Figure 2 and column 4, lines 43-67) and accelerating the synthesis steps including deprotecting steps (as taught by Williams) with microwaves (See, e.g., Cargill et al.). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods-- substantially accelerate reactions and save time as taught by Yu et al. (page 4781, column 1, lines 13-15), by Williams (Example 5) and by Cargill et al. (e.g., column 4, lines 37-39). There would have been a reasonable expectation of success, given that libraries of peptides comprising single-vessel solid phase strategies were known to successfully synthesize simultaneously (one per vessel) a multitude of different peptides in a single run (e.g.,

Cargill et al., column 1, lines 38-67 and column 2, lines 1-20). Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 2, 5, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004), in view of Williams (US 6,858,434), in view of Cargill et al. (US 6,171,555), in view of Stadler et al. (Eur J Org Chem, 2001) in view of Santagada et al. (Tetrahedron Letters, 2001, citation 4 in the IDS of November 8, 2004.

Cargill et al., Yu et al. and Williams are relied upon as above.

Cargill et al., Yu et al. and Williams do not expressly teach accelerating the deprotecting step by applying microwave energy during the deprotecting step, maintaining the peptide in a single vessel during the process proactively cooling the vessel and its contents during application of microwave energy, cleaving the peptide from the resin applying microwave energy, deprotecting side chains of the peptide, spiking the microwave energy, using phosphorium activators, uranium activators, HATU, HBTU, PyBOP, PyAOP or HOBT, monitoring the temperature of the vessel and moderating the applied power accordingly.

Stadler et al. teach cleaving various molecules including carboxylic acids from resins by applying microwave energy, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly (see, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2).

Santagada et al. teach using PyBOP/HOBt and HBTU/HOBt activators in a microwave method for peptide synthesis (see, e.g., pages 5171-5173).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the microwave method of Yu et al. by also accelerating the deprotecting steps in general during peptide synthesis with microwaves based on the teachings of Williams (See, e.g., Examples 5 and 7), by accelerating the cleavage from the solid-support resin as taught by Stadler et al. (See, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2), and by using activators such as PyBOP/HOBt and HBTU/HOBt during microwave activation, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly, as taught by Santagada et al. (See, e.g., pages 5171-5173). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods-- substantially accelerate reactions and save time (e.g., Yu et al. page 4781, column 1, lines 13-15 and Cargill et al. column 4, lines 38-40) and provide higher yields (e.g., Santagada et al. abstract). There would have been a reasonable expectation of success, given that libraries of peptides comprising single-vessel solid phase strategies were known to successfully synthesize simultaneously (one per vessel) a multitude of different peptides in a single run as taught by Cargill et al. (e.g., column 1, lines 38-67 and column 2, lines 1-20). The adjustment of particular conventional working conditions (e.g., deprotecting protective groups other than n-Boc in peptides, and alpha-amino groups or side chains of the

peptide) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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